A New Era of Vitiligo Research and Treatment

This is a very exciting phase of vitiligo research in which vitiligo is being tackled by multipronged attacks in the form of advancement in basic research, genetics and treatment including surgical management. In order to achieve the ultimate goal of total stability and complete repigmentation, there is a need to define a roadmap and roadblocks.

Vitiligo Global Issues Consensus Conference (VGICC) recently revised the classification of the disease.[1] There are still several unmet needs as pathophysiology or prognosis based classifications would be more useful. Recent progress in genetics of generalized vitiligo provide insights into underlying pathogenetic mechanisms and incrimination of vitiligo susceptibility genes that controls important aspects of immune regulation.[2] Recent data has clearly supported that vitiligo is a T-cell mediated autoimmune disease.[3,4] Heat shock protein 70 (HSP70) plays a central non redundant role in precipitating of depigmentation in vitiligo.[5] Mosenson *et al*. in a very promising study recently showed that vitiligo can be reversed through immune targeting with mutant HSP70.[6]

The bottle neck in vitiligo research is defining stability in vitiligo. Many attempts have been made to define it based on clinical, histological or immunological parameter with variable results.[7,8] It seems that disease activity in vitiligo is a dynamic process and only predictable thing about stability in non-segmental vitiligo is its unpredictability. VGICC recommends disease stability be best assessed based on the stability of individual lesions rather than the overall stability of the disease as the latter is difficult to define precisely and reliably.[1]

There are two main goals of any vitiligo treatment; first is to stop the arrest of further depigmentation and second is to induce repigmentation. The first goal can only be archived fully if we could unravel the mechanisms underlying the disappearance of melanocytes in vitiligo. If this can be achieved repigmentation should be rather simple to accomplish with a combination of medical and/or surgical treatment. Unfortunately, in the literature there are only few studies which have taken into consideration the disease activity as most of the published studies discussed repigmentation as the main outcome. Phototherapy, topical calcineurin inhibitors and topical steroids are still the mainstay of medical treatment of vitiligo. In a recent preliminary study, afamelanotide (16 mg subcutaneous implant) along with Narrowband UVB has given promising results.[9] Further, controlled studies are required to confirm its efficacy and define its role in the management of vitiligo.

Surgical methods are emerging as an important solution for stable vitiligo refractory to medical treatment. Over the years vitiligo surgery has gained steady importance with more and more improved techniques proving their effectiveness. Non-cultured epidermal cell suspension (NCES) is emerging as the first line of surgical management of stable vitiligo.[10] Major advantages of NCES are that a smaller amount of donor skin is needed to cover large recipient area, little postoperative pain and discomfort, easier placement of cellular graft, excellent color match. Mohanty *et al*. used follicular unit extraction to tap the melanocytes reservoir in the hair follicle in the surgical management of vitiligo.[11] There are many differences between epidermal and hair follicle melanocytes. Epidermal melanocytes mainly consist of a homogeneous population of highly dendritic and uniformly weakly pigmented cells, whereas hair follicle melanocyte consists of at least three distinct sub-populations, including highly pigmented/dendritic bulbar melanocytes, less-differentiated tripolar cells, and an undifferentiated amelanotic bipolar sub-population. In addition, hair follicle melanocytes expressed some

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Quick Response Code:

Website: www.jcasonline.com

DOI: 10.4103/0974-2077.112664

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antigens associated with alopecia areata, but not antigens associated with vitiligo. This could be an added advantage of repigmentation induced by using hair follicle melanocytes and long-term follow-up is required for assessing the stability of repigmentation.

In this new era of vitiligo research we are looking forward to the development of new molecules aimed at vitiligo rather than borrowing from the agents used for other diseases. New exciting options are being explored as more reservoirs of melanocytes are being unravelled like dermal stem cells.

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How to cite this article: Parsad D. A new era of vitiligo research and treatment. J Cutan Aesthet Surg 2013;6:63-4.